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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,484	09/27/2004	Yasuaki Ito	62236(46342)	5324

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 05/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/509,484	ITO ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *1-10,12-17 and 19-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/27/4;2/28/6*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group VI in the reply filed on April 12, 2006 is acknowledged.

Claims 1-10, 12-17 and 19-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 12, 2006.

Claims 11 and 18 are under examination in the instant office action.

Inventorship

2. In view of the papers filed April 12, 2006, the inventorship in this nonprovisional application has been changed by the deletion of inventor Yuko Noguchi.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Claim Objections

3. Claims 11 and 18 are objected as reciting non-elected subject matter (SEQ ID NO: 2). Appropriate action is required.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 11 and 18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial credible asserted utility or a well-established utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect. Therefore, the instant claimed method of screening a compound that changes the binding properties of that protein lacks practical utility in currently available form.

It is clear from the instant application that the protein described therein has been isolated because of its similarity to a known protein. There is little doubt that, after complete characterization, this protein and encoding DNA may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to a method of screening a compound that changes the binding properties of a protein of SEQ ID NO: 4, designated TGR7, and β-alanine or L-carnosine. It is clear from the instant application that the present invention relates to a novel human G-protein-coupled receptor (GPCR), which is shown to response to two ligands, β-alanine or L-carnosine (page 4, of the instant specification). Analysis of the pattern of tissue expression of the TGR7 reveals that it is "expressed specifically in cerebellum, dorsal root ganglion, bladder, testis, uterus etc." (middle at page 39). The specification asserts further that "[t]he ligand or the GPCR of the invention is β-alanine or L-carnosine. L-carnosine is composed of β-alanine and histidine bound thereto. β-alanine is structurally akin to glycine or GABA, which is an inhibitory neurotransmitter" (middle at page 39). Based on this reasoning, "[i]t is thus considered that the GPCR of the invention will take part in regulating neurotransmission in the central or peripheral nervous system".

In the absence of knowledge of the biological significance of this specific polypeptide, a TGR7 of SEQ ID NO: 4, there is no immediately obvious patentable use for a method of screening for its binding properties. The similarity of the disclosed polypeptide to members of GPCR family does not make the instant polypeptide useful or significant as the known polypeptides. There is no evidence of record, which associates the instant human TGR7 of SEQ ID NO: 4 with any diseases or disorders. It is a general knowledge that amino acid structure cannot necessarily predict the function of the protein: "Knowing the protein structure by itself is

insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (see Skolnick et al., Box 2 on page 36). There are numerous publications available for review that indicate that even two-amino acid substitution in a molecular structure of a protein can lead to total loss of a protein to bind a specific receptor (see, for example, Yan et al., 2000). Thus, the structural homology of the proteins of the present invention to the proteins with a known function cannot *a priori* be predictive and conclusive of a function of the claimed proteins.

Therefore, to employ the polypeptide of the instant invention in the future methods "of screening a compound that changes the binding properties" of the instant TGR7 and β-alanine or L-carnosine is not a real world utility because it would relate to a protein for which no specific biological function is known. The instant application also fails to demonstrate use of the protein as a marker for any disease or condition (which would be a real world use). Because the instant specification does not teach a biological activity of the protein, which supports a practical utility, one would not reasonably believe that the modulation of the instant polypeptide to its naturally occurring ligand, β-alanine or L-carnosine, would be useful in control of anxiety, convulsions, schizophrenia, epilepsy, psychosomatic disorders, incontinence, neurogenic hypertension, threatened abortion, male infertility, cerebrovascular disorders, polio, spastic spinal paralysis, multiple sclerosis or spinocerebellar degeneration, as implied by the specification (see middle at page 64, for example). To employ a polypeptide of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the disclosed protein then the

claimed invention, a method of screening a compound that changes the binding properties of TGR7 and β-alanine or L-carnosine, is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 11 and 18 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Claims 11 and 18 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 11 and 18 are directed to methods of using partial peptides of the disclosed polypeptide of SEQ ID NO: 4. The claims do not require that the partial peptides possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims encompass a genus of peptides that is defined only by sequence similarity. However, the instant specification fails to describe the entire genus of proteins, which are encompassed by these claims. In making a determination of whether the application complies with the written

description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a nucleic acid molecule which encodes a protein which has the amino acid sequence of SEQ ID NO: 4. The claims are drawn to methods of using "partial proteins", which are fragments of a polypeptide of SEQ ID NO: 4. Thus, the claims are not limited to use of a protein with a specific amino acid sequence. The claims only require the claimed methods to employ peptides that share some degree of structural similarity to the isolated protein of SEQ ID NO: 4. The specification only describes a protein having the amino acid sequence of SEQ ID NO: 4, which asserted to function as a novel GPCR, and fails to teach or describe any other protein which lacks the amino acid sequence of SEQ ID NO: 4 and has the activities possessed by the isolated protein.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of "partial peptide". There is not even identification of any particular portion of the structure that must be conserved. As stated above, it is not even clear what region of the encoded polypeptide has the disclosed GPCR activity. The specification does not provide a complete structure of those partial peptides encompassed by the claims. Accordingly, in the absence of sufficient recitation of distinguishing identifying

characteristics, the specification does not provide adequate written description of the recited genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of partial peptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only methods of using full length of isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 4, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-*

Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 11 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claims 11 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are at least as follows:

(1) contacting the compounds; (2) assaying the binding; (3) identifying the specific changes of binding characteristics; (4) comparison step.

Art of record

11. The art of record that discloses a polypeptide with 100% identity to the instant polypeptide of SEQ ID NO: 4 is as follows:

WO-01/66750 (2001);

WO-01/70814 (2001);

WO-01/57085 (2001);

WO-01/48188 (2001);

WO-01/36471 (2001) and

WO-01/83748 (2001); all presented in IDS submitted on 09/27/2004.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1649

May 19, 2006